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DESAL, RITA J				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/532,633

Applicant(s)

LEBLANC ET AL.

Examiner

Rita J. Desai

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2008.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-16 and 18-26 is/are pending in the application.
4a) Of the above claim(s) 22-26 is/are withdrawn from consideration.
5) ☐ Claim(s) 20 is/are allowed.
6) ☒ Claim(s) 1-3m 6-16, 18-19 and 21 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

The examiner had expanded the groups and included groups I-II in the elected groups. This would include compounds and the pharmaceutical compositions when , one of X1 or X3 is a N, X4 is CSO₂CH₃ or alkyl, Y1 is a S.

The claims have not been amended to the elected group. See for instance claim 1 page 3 of the amendment definition of Rg.

Claims pending 1-3, 6-16, 18-26.

Claims 22-26 were withdrawn as being nonelected complex compositions and method of treating claims.

The rejection over claims 4, 5, and 17 is moot as applicants have cancelled these claims. However on the claims 1-3, 6-16, and 18-21 the rejection under 35 USC first para still stands. Applicants still have all the optionally substituents off of substituents , which includes a large bulky groups being further substituted with other large bulky groups. The only substituents enabled are halogens on the Ar being a phenyl. The heteroaryl groups do not have any substituents.

The R1 and R2 substituents are also only H. In the pharmaceutical art which is so unpredictable applicants need to provided more directions. The R1 and R2 is on the ring which has a variable ring size and with all the various substituents it would require an undue amount of experimentation to make and use the compounds of the claimed invention. The claims are also

not enabled for the hydrates. Regarding hydrates:- The claims are drawn to hydrates, yet the numerous examples presented all failed to produce a hydrate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 “The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist.” The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

See *Ex parte WEIL AND SCHLICHTING*, 158 USPQ 620 (Bd. Pat. App. & Int. 1967)
And *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (M.D. Fla. 1976)
In re Prutton, 96 USPQ 147 (C.C.P.A. 1952)
In re Walker, 22 USPQ (C.C.P.A. 1934)
In Re Sus and Schaefer 134 USPQ 1962 301-310 (*affirmed*).

The rejection is being maintained and is repeated here.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

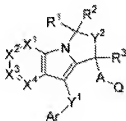
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-16, 18-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R1 and R2 to be H, R a-d superscript to be H, or Rg to be an alkyl does not reasonably provide enablement for all the various rings formed by R1 and R2 nor for other R's to be various cyclic groups and optionally substituted by other groups., Rg to be optionally substituted by other groups and then which are further substituted. And Ar to be any hetrocycle. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds with a different core and different groups hanging off of it.



The core is _____ and the various substitutes are one of X1, X2, X3 or X4 is nitrogen and the others are independently selected from CH and

C-Rg;

Y1 is selected from -(CRdRe).-X-(CRdRe)h- and X is a S.

e.g. see R_g

C 1-6alkyl optionally substituted with one to eight groups independently selected from aryl, heteroaryl, halogen, NRaRb, C(O)Ra, C(ORa)RaRb, SRa and ORa, wherein aryl, heteroaryl and alkyl are each optionally substituted with one to six groups independently selected from halogen, CF₃, and COOH,

And R^a, R^b, R^c, R^d, R^e, R^f are

R^a and R^b are independently selected from H, C1-10alkyl, C2-10alkenyl, C2-10alkynyl, Cy and Cy C1-10alkyl, wherein said alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to six substituents independently selected from halogen, amino, carboxy, C 1-4alkyl, C 1-4alkoxy, aryl, heteroaryl, aryl C 1-4alkyl, hydroxy, CF₃, OC(O)C 1-4alkyl, OC(O)NRiRj, and aryloxy; or

Ra and Rb together with the atom(s) to which they are attached form a heterocyclic ring of 4 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N-Rf;

R^c is selected from C1-6alkyl optionally substituted with one to six halogen, aryl and

heteroaryl, wherein said aryl and heteroaryl are optionally substituted with one to three groups selected from halogen, OC 1-6alkyl, O-haloC 1-6alkyl, C1-6alkyl and haloC1-6alkyl;

Rd and Re are independently H, halogen, aryl, heteroaryl, C1-6alkyl or haloC1-6alkyl;

Rf is selected from H, C 1-6alkyl, haloC 1-6alkyl, Cy, C(O)C 1-6alkyl, C(O)haloC 1-6 alkyl, and C(O)-Cy;

2) The nature of the invention: The invention is a chemical compound of a tricyclic core with 2 N's, used as a pharmaceutical to treat allergic rhinitis.

3) The state of the prior art:

How to make :-

As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they were to learn how many attempted

syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such workChemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)"

....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

Thus it is not very easy to synthesis compounds.

Similar compounds have been made however compounds with such hairy and large substituents have not been made in the prior art.

Regarding pharmaceutical applications

The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different

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substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Also the state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment of diseases as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Ex parte DIAMOND, 123 USPQ 167 (Bd. Pat. App. & Int. 1959) where the examiner was affirmed for a scope of enablement rejection, and the court stated:

Scope of claims should not be unduly extensive in chemical fields where applicability is highly speculative or not explored; subject matter which relies upon prediction for its support is unpatentable.

Specification contains 23 specific examples, but they are to preparation of relatively simple compounds; this is relatively meager and non representative disclosure to support claims embracing millions of compounds.

Applicant may not preempt unduly large field by expedient of making broad prophetic statements in specification and claims unless accuracy of such statements is sufficiently supported by well established chemical principles or by sufficient number of examples.

"The term 'substituted' without modification or restriction includes all compounds wherein one or more of the atoms or radicals of the original compound have been replaced by one or more other atoms or radicals. Without any limitation on the character or number of substituents it becomes apparent that the quoted term may be considered inclusive of almost any possible substance and the claims under consideration are either of unlimited or indeterminate scope. We are of the opinion that the reasoning of the courts in *Schering Corp. v. Gilbert*, 68 USPQ 84, and *Hercules Powder Co. v. Rohm & Haas*, 70 USPQ 297, is controlling."

embrace millions of compounds. It should also be observed that appellant is working in a field where little prediction is possible and this Board has on several occasions held that the scope of claims should not be unduly extensive in fields where applicability is highly speculative or not explored and that subject matter which relies upon prediction for its support is unpatentable. *Ex parte Middleton*, 87 USPQ 57; *Ex parte Kauck et al.*, 95 USPQ 197, *Ex parte Rosenkranz et al.*, Pat. No. 2,715,637.

In *Minnesota Mining and Mfg. Co. et al. v. Carborundum Co. et al.*, 155 F.2d 746, 69 USPQ 288, the court held that "An inventor cannot disclose a small number of components which will serve as a springboard for claiming an entire class."

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In addition

See also: *Schering Corporation v. Gilbert et al.*, 68 USPQ 84 (2d Cir. 1946)

It was shown in evidence and by way of admissions elicited by the defendants from the plaintiff before trial that one skilled in the art of organic chemistry may start in the group of the acetic acid radical and the radicals of homologues of acetic acid to which the patent relates, for instance, with the simple hydrocarbon called methane and theoretically progress along the series in the general group called alkanes from one substance to another by increasing the size of the molecules in steps of one carbon atom and two hydrogen atoms. At least formulas for such substances, as well as for others, can be written in an indefinite chain. Also it was shown that for the hydrogen atoms of the alkane molecules the atoms of what are called halogens may be substituted and so may the atoms of other groups including the residue of the hydrocarbon benzene. The latter is represented in chemical formulas by a hexagon which is called the benzene ring and, as changes in the atomic structure of the molecule occur, the ones introduced take varying positions within the ring which positions determine the nature of the compound.

Theoretically a multitude of substances not as yet found in nature and not as yet compounded could be synthesized, if skilled organic chemists were given the time and materials with which to work, and actually the formulas for them could be written. There is, however, a practical limit upon synthesis, though the extent of that is not fully known, for some of the new theoretical compounds might be impossible to create, and some would be so unstable that they would disintegrate either at once or in short periods of varying length. Moreover, while analogy is at times useful, organic chemistry is essentially an experimental science and results are often uncertain, unpredictable and unexpected.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art:

How to use:- It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the

physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no compounds made with the various substituents for R1, R2, Rg, heterocycle and also for R^{a-f}.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here. As per MPEP 2164.01 (b):

A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. In *re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

There are no starting material provided with respect to the various substituents.

7) The existence of working examples: The instant specification does not have any working examples with respect to the various substituents as given above and also no data has been provided for any compounds. Some theoretical assays are described but no activity data has been provided.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of all the above factors, guidance and state of the art, it would require an undue amount of experimentation to make the invention of the claims with various substituents, or for using them to treat or prevent the diseases i.e. Pharmaceutical compositions also. Since the art is unpredictable and since there are only a few compounds made of a very limited scope it cannot be seen how the full scope is enabled.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

“A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.”

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Double Patenting

In the event of a rejoinder applicants should be aware of the Obvious Type of Double Patenting over US 11/667346.

Conclusion

Claims 1-3, 6-16, 18-19 and 21 are not allowable.

Claims 20 may be allowable.

Claims 22-26 are withdrawn as being non-elected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Rita J. Desai/
Primary Examiner, Art Unit 1625

R.D.
December 19, 2008